

Poster presentation

## Molecular modeling studies of lipase-catalyzed $\beta$ -lactam polymerization

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Enzymatic polymerization has emerged over the last 5 years as a field of considerable interest and commercial promise. The reaction proceeds with high regio-, enantio-, and chemoselectivity under relatively mild conditions. Enzymes have been used so far to synthesize polyesters, polysaccharides, polycarbonates, polyphenols, poly-anilines, vinyl polymers, and poly-amino acids [1]. Particularly, lipase B of *Candida antarctica* immobilized on polyacrylic resin (Novozyme 435) has proven to be a very versatile catalyst and has successfully been used for the synthesis of polyesters from various substrates [2][3][4]. Little, however, has been reported on the enzyme catalyzed synthesis of polyamides [5].

While it has been shown that nylons can chemically be produced from the corresponding amino acids or by anionic ring-opening polymerization of 5–13 membered unsubstituted lactams, poly- $\beta$ -alanine has not yet been obtained by either polymerization of  $\beta$ -alanine or  $\beta$ -lactam (2-azetidinone). Using lipase B of *Candida antarctica* we have recently been successful in the production of unbranched poly- $\beta$ -alanine starting from unsubstituted  $\beta$ -lactam [6].

Here we report preliminary molecular modeling studies of the lipase catalyzed ringopening polymerization of  $\beta$ -lactam towards an understanding of the underlying enzymatic mechanism. We can show that amide formation initially follows the well-known enzymatic acylation of Ser105 by  $\beta$ -lactam using Asp187 and His224 of the catalytic centre and Thr40 and Gly106 as oxy-anion hole. The

elongation of the chain, however, utilizes different parts of the active site. The mechanism is only applicable for  $\beta$ -lactam and can not be utilized by  $\beta$ -alanine and suggests a reasoning for the experimental finding that  $\beta$ -alanine can not be polymerized enzymatically but rather inhibits the polymerization in a copolymerization experiment with  $\beta$ -lactam and  $\beta$ -alanine.

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